

UNCLASSIFIED

AD NUMBER
AD828838
NEW LIMITATION CHANGE
TO Approved for public release, distribution unlimited
FROM Distribution: Further dissemination only as directed by Office of Naval Research, ATTN: Code 429, One Liberty Center, Suite 1425, 875 North Randolph Street, Arlington, VA 22203-1995, 31 DEC 1967, or higher DoD authority.
AUTHORITY
ONR ltr dtd 28 Jul 1977

THIS PAGE IS UNCLASSIFIED

research report

AD828838

department of chemistry

AD828838

PURDUE UNIVERSITY - LAFAYETTE, INDIANA

PURDUE UNIVERSITY
DEPARTMENT OF CHEMISTRY AND PURDUE RESEARCH FOUNDATION
LAFAYETTE, INDIANA

Annual Progress Report No. 29

To: OFFICE OF NAVAL RESEARCH
Contract No. Nonr-1100 (13)

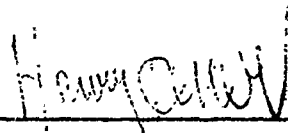
On: RESEARCH IN NITROMONOMERS AND THEIR APPLICATION TO SOLID
'SMOKELESS PROPELLANTS

For the Period: 15 September 1966 to 14 September 1967

Submitted by: Henry Feuer

Date: December 31, 1967

No. of Pages: 54


Henry Feuer

"EACH TRANSMITTAL OF THIS DOCUMENT OUTSIDE OF THE
DEPARTMENT OF DEFENSE MUST HAVE PRIOR APPROVAL OF THE
OFFICE OF NAVAL RESEARCH (CODE 429), WASHINGTON,
D. C. 20360".

TABLE OF CONTENTS

Contract Fulfillment	i
Introduction	ii
Summary	iii
Discussion	1
The Dinitration of Cyclanones in Liquid Ammonia	1
Experimental	6
Preparation of Dipotassium	
2-Keto-1,3-cyclopentanedinitronate	6
Preparation of Dipotassium	
2-Keto-1,3-cyclohexanedinitronate	6
Preparation of Dipotassium	
2-Keto-1,3-cycloheptanedinitronate	6
Discussion	8
The Mononitration of Cyclanones in Liquid Ammonia	8
Experimental	12
Standard Procedure for the Mononitration of Ketones in Liquid Ammonia .	12
Nitration of Cycloheptanone	12
Nitration of Cyclooctanone	12
Nitration of Cyclohexanone	13
Nitration of Cyclopentanone	13
Nitration of Cyclononanone	14
Nitration of Cyclodecanone	14
Nitration of Cyclododecanone	14
Nitration of Propiophenone	15

Nitration of α -Tetralone	15
Nitration of 4-Heptanone	15
Discussion	17
The Alkyl Nitration of Aliphatic and Phenylacetate Esters in Liquid Ammonia	17
Aliphatic and Aryl Aliphatic Ethyl Esters	19
Aliphatic and Aryl Alkyl <i>t</i> -Butyl Esters	22
Study of the Cleavage and Transesterification Reactions	23
Experimental	34
Alkyl Nitration of Ethyl Butyrate	34
Nitration of Ethyl Caproate without Subsequent Acidification	35
Nitration of Ethyl <i>p</i> -Methoxyphenylacetate	35
Nitration of Diethyl Homophthalate	36
Preparation of α -Bromo- α -nitrohomophthalimide	37
Treatment of Ethyl α -Nitrocaproate with Potassium Ethoxide at Alkyl Nitrate Nitration Conditions	37
Preparation of Potassium 1-Carbethoxy-1-pentanenitronate	37
Conversion of Potassium 1-Carbethoxy-1-pentanenitronate to Ethyl α - Nitrocaproate	38
Nitration of <i>t</i> -Butyl Caproate	38
Addition of "Solid Potassium Ethoxide" Prior to Butyl Nitrate in the Nitration of <i>t</i> -Butyl Caproate in Liquid Ammonia	39
Treatment of a Mixture of Ethyl α -Nitrocaproate and <i>t</i> -Butyl α - Nitrocaproate with Potassium Ethoxide at Alkyl Nitrate Nitration Conditions	40
Treatment of a Mixture of Ethyl and <i>t</i> -Butyl α -Nitrocaproates with Ethanolic Acetic Acid	40
Conversion of <i>t</i> -Butyl Caproate to Ethyl Caproate in Potassium Amide- Liquid Ammonia	40

Transesterification Between <i>n</i> -Butyl Nitrate and "Solid Potassium Ethoxide" at Conditions of the Alkyl Nitrate Nitration	41
---	----

Table I

Alkyl Nitrate Dinitration of Cyclanones in Potassium <i>t</i> -Butoxide - Tetrahydrofuran and Potassium Amide-Liquid Ammonia	3
--	---

Table II

Effect of Time for Anion Formation and Base Concentration on the Alkyl Nitrate Dinitration of Cyclanones	5
--	---

Table III

Alkyl Nitrate Mononitration of Ketones in Potassium <i>t</i> -Butoxide- Tetrahydrofuran and Potassium Amide-Liquid Ammonia	9
--	---

Table IV

Effect of Base and Alkyl Nitrate Concentrations on the Mononitration of Cyclanones	11
--	----

Table V

Alkyl Nitrate Nitration of Ethyl Esters	20
---	----

Table VI

Alkyl Nitrate Nitration of <i>t</i> -Butyl Esters	24
---	----

Table VII

Physical Properties of <i>t</i> -Butyl α -Nitroesters	26
--	----

Table VIII

Spectral Data of <i>t</i> -Butyl α -Nitroesters	27
--	----

Table IX

Spectral Data of Ethyl α -Nitroesters	28
--	----

Distribution List	42
-----------------------------	----

Contract Fulfillment

This report is submitted in partial fulfillment of Contract No. Nonr-1100 (13).

Introduction

This report covers work carried out under Contract No. Nonr-1100 (13) during the period 15 September 1966 to 14 September 1967. Previous work is presented in Purdue Progress Reports one to twenty-eight.

Summary

1. The general utility of the alkyl nitrate nitration for introducing nitro groups into active methylene compounds has been further advanced. It has now been discovered that the potassium t-butoxide-tetrahydrofuran system (A), which has been used as the base-solvent combination in these reactions, can be readily replaced by the potassium amide-liquid ammonia system (B).

In system (B), the dinitration as well as mononitration of cyclanones has given the salts of α,α -dinitrocyclanones and α -nitrocyclanones in yields which are comparable with those obtained in system (A).

2. In system (A), mononitration of cyclanones has been found to give α -nitrocyclanones and the cleavage products, ω -nitrocarboxylic esters, the ratio of which varied with ring size. The mononitration follows a similar course in system (B) but the amount of ring cleavage is decreased.

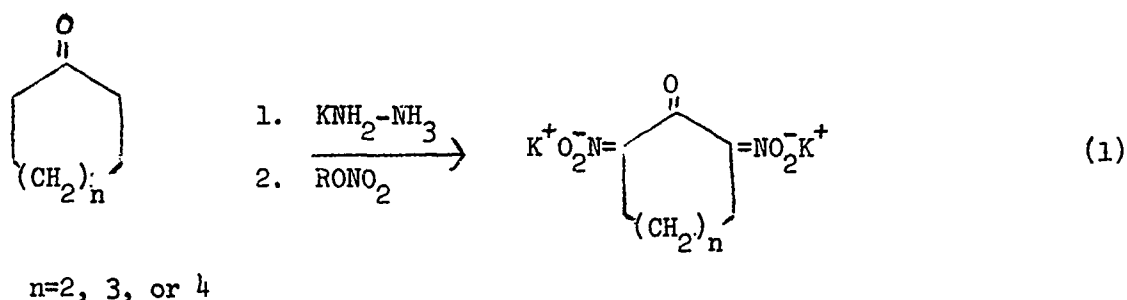
3. The alkyl nitration of aliphatic and phenylacetate esters in the potassium amide-ammonia system has been found to lead to α -nitroesters in good yields, while in the potassium t-butoxide-tetrahydrofuran system, the yields are very low.

In addition to the α -nitroesters, fragmentation products, such as nitroalkanes and alkyl carbonates, were obtained, which formed during the nitration step and not during workup.

DISCUSSION

The Dinitration of Cyclanones in Liquid Ammonia

In continuation of our studies of the alkyl nitrate nitration of active methylene compounds, we are now reporting a substantial improvement over the previously employed procedure, in which nitrations with alkyl nitrates were carried out in a tetrahydrofuran (THF)-potassium *t*-butoxide system (A) at about -50°C .^{*} The time consuming preparation of anhydrous peroxide-free THF and sublimed potassium *t*-butoxide has now been eliminated by performing nitrations in the potassium amide-liq. ammonia system (B). Although reactions in system (B) have been observed to be heterogeneous, the nitrations of the $\text{C}_5\text{-C}_7$ cyclanones gave the corresponding dipotassium 2-keto-1,3-cycloalkanedinitronates (1) in yields which were comparable or better than those in system (A) (eq. 1).



A comparison of the data is presented in Table I. The yields of $\alpha, \alpha', \omega, \omega'$ -tetrabromo-

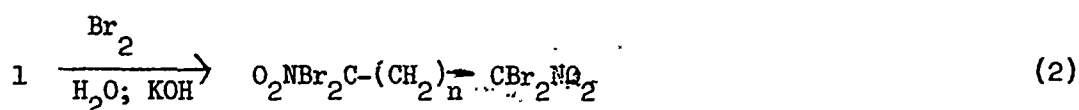
*H. Feuer, J. W. Shepherd and C. Savides, *J. Amer. Chem. Soc.*, **78**, 4364 (1965).

H. Feuer and C. Savides, *ibid.*, **81**, 5826 (1959).

H. Feuer and B. F. Vincent, Jr., *J. Org. Chem.*, **29**, 939 (1964)

H. Feuer and P. M. Pivawer, *ibid.*, **31**, 3152 (1966).

α,ω -dinitroalkanes* which arise from the aqueous bromination of the dinitro disalt, are included (eq. 2) because a reliable method for purifying dipotassium 2-keto-1,3-cycloheptanedinitronate (1, $n=4$) has been found only recently.



$n=2, 3, \text{ or } 4$

It is quite apparent that the amount of dinitration cannot be based on the ring opening reaction brought about by alkaline bromination because the reaction is far from being quantitative.

The importance of reaction temperature, time of anion formation, and concentration of base on the yield of dinitro compounds was studied, and the results are summarized in Table II.

In the case of cyclopentanone and cyclohexanone, it was found that higher yields were obtained when alkyl nitrations were performed at -33° rather than -50° . Since these reactions are heterogeneous, these results reflect the faster rate at which anion formation occurs with increasing temperature.

A time of 30 minutes was found to be sufficient for complete anion formation with cyclopentanone and cyclohexanone. With cycloheptanone, at the same reaction conditions, anion formation was incomplete because extension of the time from 30 minutes to 2 hours gave a 10% increase in the yield of dinitration. But when the amount of base was increased from 2 equivalents to three, 30 minutes was sufficient for anion formation.

The data also indicate that for cyclohexanone and cycloheptanone the amount of dinitration is increased with larger potassium amide concentrations. Since the extent

* K. Klager, J. Org. Chem., 20, 646 (1955).

Table I

Alkyl Nitrate Dinitration of Cyclanones in Potassium t-Butoxide-
THF and Potassium Amide-Liquid Ammonia^a

Ketone	K-t-OBu-THF		KNH ₂ -NH ₃	
	Bromination Product ^b Yield %	Disalt ^c Yield %	Bromination Product ^b Yield %	Disalt ^c Yield %
Cyclopentanone	72	98.5	88.8	94.2
Cyclohexanone	53	74.6	51.8 ^d	94.5
Cycloheptanone	54	-	80.5	85.2

^aIn both systems amyl nitrate was the nitrating agent.

^bBromination product is $\alpha,\alpha,\omega,\omega'$ -tetrabromo- α,ω -dinitroalkane.

^cDisalt is dipotassium 2-keto-1,3-cycloalkanedinitronate.

^dObtained from the bromination of crude dipotassium 2-keto-1,3-cyclohexanedinitronate.
Yield based on cyclohexanone.

of nitration is dependent upon anion formation, the data suggest that the acidity of the C_5-C_7 cyclanones varies with ring size and is highest in the case of cyclopentanone.

The importance of the amount of base on the amount of dinitration is further indicated by the results which were obtained when cycloheptanone and cyclooctanone were nitrated with 2 equivalents of potassium amide and 2.2 equivalents of amyl nitrate. In addition to the dinitro salts, there were also isolated after acidification with glacial acetic acid, 2-nitrocycloheptanone (25.3%) and 2-nitrocyclooctanone (55.8%).

The formation of mononitro compounds is a good indication that dinitration proceeds in a stepwise fashion. Conversion of 2-nitrocyclooctanone to dipotassium 2-keto-1,3-cyclooctanedinitronate in 28% support this contention (eq. 3).

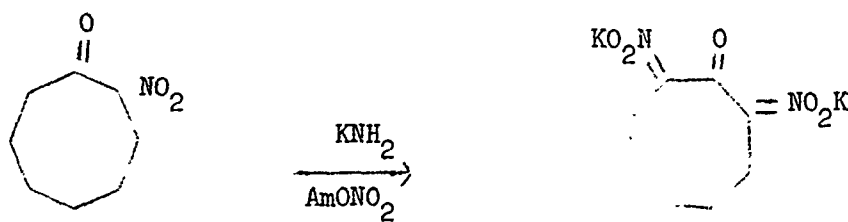


Table II

Effect of Time for Anion Formation and Base Concentration on
the Alkyl Nitrate Dinitration of Cyclanones^a

<u>Ketone</u>	<u>Contact Time^b</u> <u>(Hrs.)</u>	<u>KNH₂</u> <u>(Equivs.)</u>	<u>Disalt^c</u> <u>Yield %</u>
Cyclopentanone	0.5 ^d	2.0	88.4
Cyclopentanone	0.5	2.0	94.2
Cyclohexanone	0.5 ^d	2.0	53.4
Cyclohexanone	0.5	2.0	72.7
Cyclohexanone	2.0	2.0	76.1
Cyclohexanone	0.5	3.0	94.5
Cycloheptanone	0.5	2.0	61.7 ^e
Cycloheptanone	2.0	2.0	73.3 ^{e,f}
Cycloheptanone	0.5	3.0	72.9
Cycloheptanone	0.5	3.5	85.2

^aIn all cases the ratio of KNH₂ to RONO₂ was approximately one.

^bThe time at which the ketone and base were allowed to interact before the nitrate was added. The temperature was -33° unless noted otherwise.

^cDipotassium 2-keto-1,3-cycloalkanedinitronate.

^dThe reaction temperature was -50°.

^eYield of dinitronate salt calculated from the amount of 1,6-dinitrohexane obtained from the acid cleavage of the crude salt. The cleavage is known to proceed in 91% yield.

^fA 25.3% yield of α-nitrocycloheptanone was also obtained.

EXPERIMENTAL

Dipotassium 2-Keto-1,3-cyclopentanedinitronate. - Cyclopentanone (4.32 g., 0.051 mole) was added dropwise over 15 minutes to a solution of potassium amide (0.103 mole) in 200 ml. liquid ammonia at -33° . After stirring the mixture for 0.5 hour, amyl nitrate (15.07 g., 0.113 mole) was added dropwise over 10 minutes. The reaction mixture was then allowed to stir 0.5 hour at -33° , 100 ml. of anhydrous ether was added and the ammonia allowed to evaporate. Filtering and drying in vacuo gave 12.91 g. of crude disalt.

Dissolving 7.94 g. of the disalt in a minimum amount of water, reprecipitating with methanol, by dropwise addition, filtering and drying in vacuo gave 7.48 g. (94.2%) of dipotassium 2-keto-1,3-cyclopentanedinitronate, neut. equiv. found 126; calcd. 125.

Dipotassium 2-Keto-1,3-cyclohexanedinitronate. - The experimental procedure was similar to that of the dinitration of cyclopentanone except that the amyl nitrate was added over a period of 20 minutes.

Dissolving the crude nitration product in a mixture of water and methanol (1:1), and precipitating with acetone gave after filtering and drying 14.2 g. of crude disalt. Repeating the purification procedure gave 12.7 g. (94.5%) dipotassium 2-keto-1,3-cyclohexanedinitronate, neut equiv. found 131; calcd. 132.

Dipotassium 2-Keto-1,3-cycloheptanedinitronate. - The experimental procedure was similar to that of the dinitration of cyclopentanone except that the amyl nitrate was added over a period of 20 minutes.

After allowing the reaction mixture to attain room temperature and removing the ether in vacuo, the residue was dissolved in 400 ml. of methanol. Reprecipitating the salt with ether, filtering, and drying in vacuo gave 15.1 g. (85.2%) of dipotassium 2-keto-1,3-cycloheptanedinitronate, m.p. $180-190^{\circ}$ (dec.); $\lambda_{\text{max}}^{\text{Nujol}}$ 1600 cm^{-1} (C=O), 1225 cm^{-1} (C=NO₂⁻, asym. stretch), 1126 cm^{-1} (C=NO₂⁻ sym. stretch);

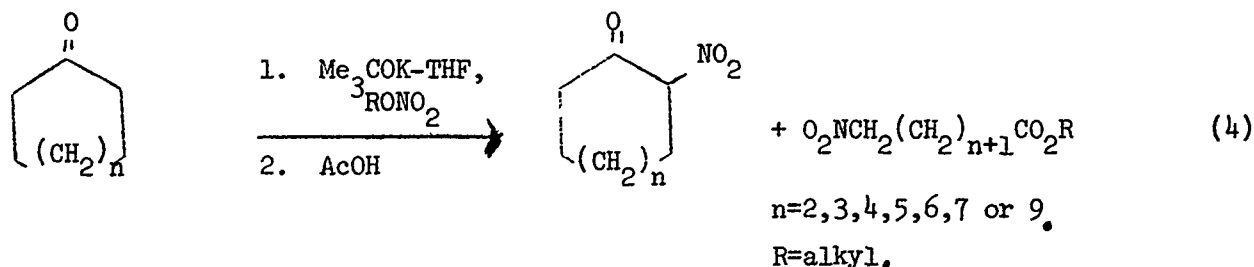
n.m.r. D_2O 2.26 ($CH_{2\beta}$, multiplet) and 1.67 ppm. ($CH_{2\gamma}$, multiplet).

Anal. Calcd. for $C_{17}H_{18}N_2O_5K_2$: C, 30.22; H, 2.88; N, 10.08; K, 28.13; neut. equiv. 139. Found: C, 29.42; H, 3.13; N, 10.13; K, 27.89; neut equiv. 139.

DISCUSSION

The Mononitration of Cyclanones in Liquid Ammonia

Mononitration of ketones has previously been successfully carried out in the potassium t-butoxide-THF system (A) and it was reported that the reaction gave, in addition to α-nitroketones, carboxylic esters which in the case of cyclanones were proven to be ω-nitrocarboxylic esters* as shown in eq. 4.



When the mononitration of ketones was investigated in the potassium amide-ammonia system (B), the qualitative results were found to be the same as in system (A) in that α-nitroketones and carboxylic esters were isolated. However, as seen in Table III, less of the cleavage product was obtained even with the highly strained eight and nine-membered cyclanones. The case of cyclopentanone warrants special mention because as in system (A), dinitration prevailed and no α-nitrocyclopentanone was obtained. Only a small amount of mononitration was detected by isolation of the cleavage product amyl 5-nitropentanoate in 11% yield.

In order to determine conditions for optimum yields of mononitration, the influence of potassium amide and alkyl nitrate concentrations were studied. The results, which are summarized in Table IV show that excess of base is detrimental to the yield of α-nitroketones, while an excess of alkyl nitrate over the base is

* H. Feuer and P. M. Pivawer, J. Org. Chem., 31, 3152 (1966)

Table III

Alkyl Nitrate Mononitration of Ketones in

Potassium t-Butoxide-THF and Potassium Amide-Liquid Ammonia

<u>Ketone</u>	<u>α-Nitroketone</u>		<u>ω-Nitrocarboxylic Ester</u>	
	<u>(A)</u> ^a	<u>(B)</u> ^b	<u>(A)</u>	<u>(B)</u>
Cyclopentanone	c	c	10	11
Cyclohexanone	20	59	10	2
Cycloheptanone	65	79	4	1
Cyclooctanone	35	60	37	22
Cyclononanone	14	27	60	46
Cyclodecanone	14	17	58	50
Cyclododecanone	54	64	23	17
Propiophenone	16	30	d	0
α -Tetralone	59	71	0	0
4-Heptanone	39	55	e	f

^aPotassium t-butoxide (1.65 equivs.) and alkyl nitrate (1.1 equivs.) in THF at -50° were employed.

^bPotassium amide (1 equiv) and alkyl nitrate (2 equivs.) in ammonia were employed at -33°. Two hours were allowed for anion formation except in the case of cyclohexanone where only 1 hour was allowed.

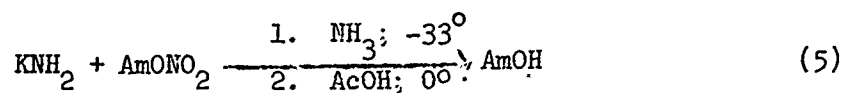
^cDipotassium 2-keto-1,3-pentanedinitronate was obtained in (A) and (B) in yields of 19% and 29%, respectively. Also, the aldol condensation product 2-(1-hydroxycyclopentyl) cyclopentanone was obtained in both systems (A) and (B).

^dEthyl benzoate and benzoic acid were obtained in yields of 8% and 7%, respectively.

^eAmyl butyrate (25%) and 1-nitropropane (20%) were obtained.

^fEthyl butyrate (7.4%) and 1-nitropropane (7.5%) were isolated.

required for optimum yields. An excess of alkyl nitrate is required because it is solvolyzed by potassium amide at the conditions of the nitration experiment. In a control experiment in which potassium amide in ammonia and amyl nitrate were allowed to react at -33° , amyl alcohol was obtained after acidification of the reaction mixture at 0° with glacial acetic acid (eq. 5).



A similar dependence on base and alkyl nitrate concentrations has been observed in the dinitration of ketones (vide supra).

Table IV

Effect of Base and Alkyl Nitrate Concentrations
on the Mononitration of Cyclanones

Ketone ^a	KNH ₂ (equivs.)	RONO ₂ (equivs.)	<u>α-Nitrocyclanone</u>	<u>ω-Nitrocarboxylic</u>
			Yield %	Ester Yield %
Cycloheptanone	2	1.1 ^b	3	0
Cycloheptanone	1	1.1 ^b	62	0
Cycloheptanone	1	2.0 ^b	79	1
Cyclooctanone	1	1.1 ^b	54	19
Cyclooctanone	1	2.0 ^b	60	22
Cyclodecanone	1	1.1 ^c	6	30
Cyclodecanone	1	2.2 ^c	17	50

^aIn all experiments the ketone was added to the base at -33° and 2 hours were allowed for anion formation. Then the alkyl nitrate was added in 10 minutes at -40°.

^bAmyl nitrate was the nitrating agent.

^cEthyl nitrate was the nitrating agent.

EXPERIMENTAL

Standard Procedure for the Mononitration of Ketones in Liquid Ammonia

Nitration of Cycloheptanone.- Cycloheptanone (12.9 g., 0.115 mole) was added dropwise over 10 minutes to a solution of potassium amide (0.115 mole) prepared with potassium (4.5 g., 0.115 g. at.) in 300 ml. liquid ammonia at -33° in the presence of a catalytic amount of ferric nitrate decahydrate. After stirring the mixture for 2 hours, amyl nitrate (26.7 g., 0.21 mole) was added over 10 minutes at -45° . After allowing the mixture to stir for 0.5 hours at -33° , 100 ml. of anhydrous ether was added while the ammonia was evaporated in a stream of nitrogen. Recooling to -33° , acidifying slowly with gl. acetic acid (23.1 g., 0.385 mole), stirring at 0° for 12 hours, and filtering left an oil. Distilling at 0.2 mm. gave 14.2 g. (79%) α -nitrocycloheptanone, b.p. $100-105^{\circ}$ and 0.32 g. (1.1%) amyl 7-nitroheptanoates,* b.p. 120° . The α -nitrocycloheptanone solidified on cooling and was recrystallized from isopropyl alcohol, m.p. $38-38.5^{\circ}$, lit.,** m.p. $37.5-38.0^{\circ}$. About 7% unreacted cycloheptanone was present in the Dry Ice trap as determined by glpc.

Nitration of Cyclooctanone.- The procedure was similar to that employed for the nitration of cycloheptanone. The following reactants were employed: potassium (4.20 g., 0.107 g. at.) cyclooctanone (13.53 g., 0.107 mole), amyl nitrate (26.87 g., 0.201 mole), and gl. acetic acid (28.5 g., 0.47 mole).

Distillation of the residual oil at 0.1 mm. gave 10.91 g. (59.5%) α -nitrocyclooctanone, b.p. $100-105^{\circ}$, n_D^{20} 1.5034, lit.** n_D^{20} 1.5038, and 6.04 g. (21.7%) amyl

* A mixture of isomeric esters was obtained because the nitrating agent consisted of a mixture of n-amyl and isoamyl nitrate.

** H. Feuer and P. M. Pivawer, J. Org. Chem., 31, 3152 (1966).

8-nitrooctanoates, b.p. 140-150°. The material in the Dry Ice trap contained 10% unreacted cyclooctanone as determined by glpc.

Nitration of Cyclohexanone. - The procedure was similar to that employed for the nitration of cycloheptanone, except that only 1 hour was allowed for anion formation. The following reactants were used: potassium (2.35 g., 0.06 g. at.), cyclohexanone (5.90 g., 0.06 mole), amyl nitrate (10.90 g., 0.12 mole), and gl. acetic acid (12 g., 0.20 mole).

Distilling the filtrate at 0.02 mm. gave 5.1 g. (59%) α -nitrocyclohexanone, b.p. 70-75° and 0.13 g. (1.2%) amyl 6-nitrohexanoates, b.p. 95-110°. Unreacted cyclohexanone (24%) was present in the Dry Ice trap as determined by glpc.

The α -nitrocyclohexanone solidified on standing and was recrystallized from isopropyl alcohol, m.p. 38.5-39.5°, lit.* m.p. 37°.

Nitration of Cyclopentanone. - The procedure was similar to that employed for the nitration of cycloheptanone. The following reactants were employed: potassium (4.07 g., 0.104 g. at.), cyclopentanone (15.09 g., 0.113 mole), amyl nitrate (15.9 g., 0.113 mole), and gl. acetic acid (22.5 g., 0.3 mole).

The reaction mixture was filtered to give a yellow solid.

Distilling the filtrate at 0.2 mm. gave 0.39 g. (4.6%) 2-(1-hydrocyclopentyl) cyclopentanone, b.p. 62-64° and 2.51 g. (11%) amyl 5-nitropentanoates, b.p. 100 - 104°. About 40% unreacted cyclopentanone identified by glpc was present in the Dry Ice trap.

Dissolving the yellow solid in a minimum amount of aq. potassium hydroxide (pH 11), adding an equal amount of methanol and then acetone dropwise, gave after filtering and drying in vacuo 7.58 g. (29.1%) dipotassium 2-keto-1,3-cyclopentane-dinitronate, expl. pt. 257°.

* H. Wieland, P. Garbsch, and J. J. Chavan, Justus Liebigs Ann. Chem., 461, 295 (1928).

Nitration of Cyclononanone.— The procedure was similar to that employed for the nitration of cycloheptanone. The following reactants were employed: potassium (1.31 g., 0.034 g. at.), cyclononanone (4.7 g., 0.034 mole), ethyl nitrate (6.14 g., 0.067 mole), and gl. acetic acid (8.66 g., 0.143 mole).

Distilling the residual oil at 0.01 mm. gave two fractions, b.p. 85-90° and 90-95°. Analysis of each fraction by glpc on a SF-96 on chromosorb column at 175° showed that 1.65 g. (26.6%) α -nitrocyclanone and 3.50 g. (45.5%) ethyl 9-nitrononanoate were obtained.

Nitration of Cyclodecanone.— The procedure was similar to that employed for the nitration of cycloheptanone. The following reactants were employed: potassium (2.06 g., 0.053 g. at.), cyclodecanone (8.12 g., 0.053 mole), ethyl nitrate (9.57 g., 0.11 mole), and gl. acetic acid (14.0 g., 0.233 mole).

Distilling the residual oil at 0.07 mm. gave two fractions, b.p. 115-118° and 118-120°. Glpc analysis of each fraction on a SF-96 chromosorb column at 175° showed that 1.76 g. (17.0%) α -nitrocyclodecanone and 6.39 g. (49.6%) ethyl 10-nitrodecanoate were present.

Nitration of Cyclododecanone.— The procedure was similar to that employed for the nitration of cycloheptanone. The following reactants were employed: potassium (1.63 g., 0.042 g. at.), cyclododecanone (7.58 g., 0.042 mole), ethyl nitrate (7.54 g., 0.083 mole), and gl. acetic acid (12 g., 0.2 mole).

Filtering the reaction mixture and evaporating the solvent left a residue which solidified upon cooling. Subliming at 0.6 mm. gave 0.61 g. (8%) of starting ketone. Further sublimation at 0.005 mm. gave 6.11 g. (64%) α -nitrocyclododecanone, m.p. 74-75°. Recrystallizing from isopropyl alcohol gave an analytically pure sample, m.p. 78-79°, lit.* m.p. 78-79.5°.

* H. Feuer and P. M. Pivawer, J. Org. Chem., 31, 3152 (1966).

Taking up the residue which remained after sublimation in ether, filtering, evaporating the solvent, and distilling at 0.03 mm. gave 2.63 g. (23%) ethyl 12-nitrododecanoate, b.p. 110-114°; $\lambda_{\text{max}}^{\text{Neat}}$ 1740 cm.⁻¹ (C=O), 1560 cm.⁻¹ and 1380 cm.⁻¹ (NO₂).

Nitration of Propiophenone. - The procedure was similar to that employed for the nitration of cycloheptanone. The following reactants were employed: potassium (2.18 g., 0.056 g. at.), propiophenone (7.45 g., 0.056 mole), ethyl nitrate (10.2 g., 0.112 mole), and gl. acetic acid (15.0 g., 0.25 mole).

Distilling at 0.2 mm. gave 4.27 g. (57%) starting ketone, b.p. 40° and 3.02 g. (30%) 2-nitro-1-propiophenone, b.p. 92-98°, n_D^{20} 1.5427, lit.* n_D^{20} 1.5432.

Nitration of α -Tetralone. - The procedure was similar to that employed for the nitration of cycloheptanone. The following reactants were employed: potassium (1.50 g., 0.038 g. at.), α -tetralone (5.60 g., 0.038 mole), ethyl nitrate (6.99 g., 0.07 mole), and formic acid (20 g., 0.43 mole).

Distilling at 0.2 mm. afforded 0.99 g. (18%) recovered α -tetralone and 5.13 g. (71%) 2-nitro-1-tetralone, b.p. 125-130°. The latter solidified on cooling and after recrystallizing from isopropyl alcohol had m.p. 70-71°, lit.* m.p. 72-72.5°.

Nitration of 4-Heptanone. - The procedure was similar to that employed for the nitration of cycloheptanone. The following reactants were employed: potassium (1.92 g., 0.049 g. at.), 4-heptanone (5.65 g., 0.049 mole), ethyl nitrate (8.91 g., 0.089 mole), and gl. acetic acid (12 g., 0.20 mole).

Distilling the residual oil at 0.1 mm. gave 4.25 g. (55%) 3-nitro-4-heptanone, b.p. 40-45°. Glpc on a SF-96 on chromosorb column gave the analytical sample, n_D^{20} 1.4390, lit.* n_D^{20} 1.4395.

The Dry Ice trap contained 8% starting ketone and the fragmentation products, namely 7.4% ethyl butyrate and 7.5% 1-nitropropane.

* H. Feuer and P. M. Pivawer, J. Org. Chem., 31, 3152 (1966).

Reaction of Potassium Amide with Amyl Nitrate in Liquid Ammonia - The procedure was similar to that employed for the nitration of cycloheptanone, except no ketone was used and acidification was carried out first with ammonium chloride at -33° and then with gl. acetic acid at 0° . The following reactants were employed: potassium (3.91 g., 0.10 g. at.), amyl nitrate (14.63 g., 0.11 mole), ammonium chloride (8.5 g., 0.142 mole), and gl. acetic acid (20 g., 0.33 mole).

Distilling the residual oil at 0.6 mm. gave 5.91 g. (40%) recovered amyl nitrate and 4.78 g. (49.5%) isomeric amyl alcohols both of which were identified by glpc comparison of retention times with authentic samples.

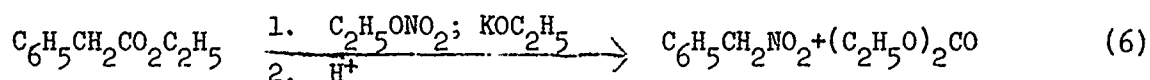
A control test in which amyl nitrate in liquid ammonia was treated with ammonium chloride at -33° and then with gl. acetic acid at 0° resulted in a quantitative recovery of the nitrate.

DISCUSSION

The Alkyl Nitration of Aliphatic and Phenylacetate Esters in Liquid Ammonia

In continuation of our studies of the alkyl nitrate nitration, we are now reporting on its application to the preparation of α -nitroesters.

Attempts by Wislicenus and coworkers*,** to prepare ethyl α -nitrophenylacetate with ethyl nitrate in the presence of potassium ethoxide led only to phenylnitromethane and diethyl carbonate (eq. 6). However, Baker*** was able to isolate ethyl



α -nitrophenylacetate by essentially following Wislicenus procedure, although no yield was reported.

Attempts to apply the alkyl nitrate nitration to aliphatic esters have largely been unsuccessful. Emmons and Freeman**** have used acetone cyanohydrin nitrate as a nitrating agent in the presence of 100% excess sodium hydride, but have found the reaction only applicable to malonic and acetoacetic esters.

In this investigation, the alkyl nitration of esters was investigated in such systems as potassium *t*-butoxide-THF, potassium *t*-butoxide-dimethylformamide, and potassium amide-liquid ammonia. Of these, only the latter was found to be useful in regard to workup and yield. It was found that the reaction gave not only α -nitroesters but also fragmentation products, namely nitroalkanes and dialkyl carbonates. Moreover, in cases where the carboxylic ester and alkyl nitrate were

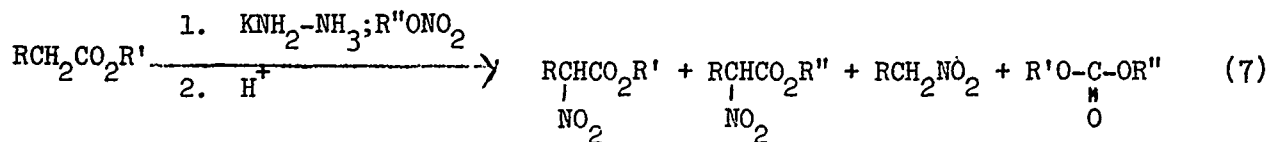
* W. Wislicenus and A. Endres, Chem. Ber., 35, 1755 (1902).

** W. Wislicenus and R. Grützner, Ibid., 42, 1930 (1909).

*** J. W. Baker, J. Chem. Soc., 1 (1935).

**** W. Emmons and J. Freeman, J. Amer. Chem. Soc., 77, 4391 (1955).

derived from different alcohols, another α -nitroester was obtained which apparently resulted from a transesterification reaction (eq. 7).



In order to determine optimum conditions for obtaining highest yields, various reaction parameters were studied with ethyl caproate and *t*-butyl caproate. A tertiary ester was chosen because ethyl caproate was partially converted to the amide and it had been established* that nucleophilic attack on the carbonyl group of a *t*-butyl ester is hindered. Because of amide formation, only a 10% excess of potassium amide could be employed in the conversion of ethyl esters to their anions. In the case of the *t*-butyl esters, a 100% excess of potassium amide could be used. This resulted in more anion formation and in a greater amount of overall nitration, as can be seen by comparing the data in Tables V and VI.

With regard to the nitrating agent, it was established that yields were highly improved when (1) a 50% excess of the alkyl nitrate over the ester was employed, (2) the addition of the alkyl nitrate was very fast, and (3) the reaction temperature during the addition was kept below -33° . The rapid addition of the nitrate is apparently necessary to prevent the conversion of any unreacted ester anion to the ester by the nitroester itself or by an intermediate which forms during the alkyl nitration.

Acidification of the salts of the nitro compounds was found to be best with gl. acetic acid after the ammonia was replaced by anhydrous ether. When ammonium chloride was used as the acidification agent*, lower yields were obtained because some of the nitro compound remained as the ammonium salt.

* C. R. Hauser, R. Levine, and R. F. Kibler, *J. Amer. Chem. Soc.*, **68**, 26 (1946)

Aliphatic and Aryl Aliphatic Ethyl Esters

As shown in Table V, the alkyl nitration of ethyl esters led to the corresponding α -nitroesters and nitroalkanes, the latter arising from a fragmentation reaction. Amide formation was only significant with the aliphatic esters. In the case of the phenyl acetates where no amide was formed, the nucleophilic attack of amide ion on the alpha-hydrogen was apparently faster than on the carbonyl carbon.

Alkyl nitration of ethyl propionate gave lower yields than of other ethyl ester because part of the ester underwent self-condensation to ethyl α -propionyl-propionate.

The importance of the acidity of the starting ester on the success of the alkyl nitration can be seen by comparing the results concerning the phenylacetates. The highest yield of overall nitration occurred with the least acidic ethyl *p*-methoxyphenylacetate, and no nitration occurred at all with ethyl *p*-nitrophenylacetate. Diethyl malonate and diethyl methylmalonate also failed to undergo nitration. On the basis of these results, it seems that the alkyl nitration in the potassium amide-ammonia system would be successful only with compounds of pK_a higher than 16.*,**

Nitration of diethyl homophthalate gave instead of the expected α -nitroester, potassium homophthalimidonitronate (2). The structure was determined by elemental analysis and infrared spectrum $\{3425 \text{ cm.}^{-1}(\text{NH}); 1689 \text{ cm.}^{-1} \text{ and } 1661 \text{ cm.}^{-1}(\text{C=O})\}$ ***. Compound 2 was converted to α -bromo- α -nitro-homophthalimide(3) (eq. 8), which according to infrared and n.m.r. spectral data had the imide structure 3. Compound 3 was unstable and slowly gave off oxides of nitrogen. Therefore it was impossible to

* R. G. Pearson and R. L. Dillon, *J. Amer. Chem. Soc.*, **75**, 2441 (1953), report that the acidity of diethyl malonate and diethyl methylmalonate lies in the range of 15-16 pK_a units.

** Most likely the reaction between ester anion and alkyl nitrate is reversible and with carbanions of acidic esters the position of the equilibrium lies far to the left.

*** Compound 2 was insoluble in solvents commonly used in n.m.r. determinations.

Table V

Alkyl Nitrate Nitration of Ethyl Esters

Ester ^a RCH ₂ CO ₂ C ₂ H ₅ , R	α -Nitroester Yield %	Nitroparaffin ^b Yield %	Acid Amide ^c Yield %	Total Nitration ^d Yield %
n-C ₄ H ₉ -	42.0 ^e	13.5 ^f	1.0 ^g	55.5 ^h
C ₂ H ₅ -	41.0 ⁱ	14.0 ^j	7.0 ^k	55.0 ^j
CH ₃ -	24.0 ^l	18.9 ^m	7.5 ⁿ	42.9 ^{h,o}
p-CH ₃ O-C ₆ H ₄ -	72.0 ^p	21.7 ^p	0	93.7
C ₆ H ₅ -	22.8 ^q	48.5 ^r	0	71.3
o-C ₂ H ₅ O ₂ C-C ₆ H ₄ -	18.9 ^s	30.6 ^t	0	49.5 ^u
p-NO ₂ -C ₆ H ₄ -	0	0	0	0

^aNitrations were carried out in the presence of potassium amide-liquid ammonia at -33° with ethyl nitrate.

^bThis is the expected cleavage product resulting from decarboxylation of the α -nitroester. In most cases the other product of decarboxylation, dialkyl carbonate, was not isolated.

^cThe acid amide results from ammonolysis of the starting ester.

^dTotal nitration represents the sum of α -nitroester and nitroparaffin.

^eB.p. 56-59° at 0.15 mm., n_D^{20} 1.4302; W. Emmons and J. Freeman, *J. Amer. Chem. Soc.*, **77**, 4391 (1955) reported b.p. 61-63° at 0.5 mm. n_D^{20} 1.4300.

^f n_D^{20} 1.4174; L. Henry {*Rec. Trav. Chim.*, **24**, 352 (1905)} reported n_D^{20} 1.4175.

^gM.p. 98-100°; W. Kelbe {*Ber.*, **16**, 1200 (1883)} reported m.p. 98-101°.

^hApproximately 20-30% of the starting ester was recovered.

ⁱB.p. 58-62° at 1.5 mm., n_D^{20} 1.4238; W. Emmons and J. Freeman, *J. Amer. Chem. Soc.*, **77**, 4391 (1955) reported b.p. 50-52° at 0.5 mm., n_D^{20} 1.4239.

^j_D²⁰ 1.4010; lit. ⁿ_D²⁰ 1.4015 {"Handbook of Chemistry and Physics," 39th ed., Cleveland Rubber Publishing Co., Cleveland, Ohio, 1957, p. 845.

^k M.p. 115-116°; lit. m.p. 116° {Ibid., p. 835}.

^l B.p. 58-61° at 2.5 mm., ⁿ_D²⁰ 1.4206; W. Emmons and J. Freeman, J. Amer. Chem. Soc., 77, 4391 (1955) reported b.p. 46° at 5 mm., ⁿ_D²⁰ 1.4208.

^m_D²⁰ 1.3918; lit. ⁿ_D^{23.5} 1.3901 {"Handbook of Chemistry and Physics," 39th ed., Cleveland Rubber Publishing Co., Cleveland, Ohio 1957, p. 917.

ⁿ M.p. 75-77°; lit. m.p. 78-79° {Ibid., p. 1129}.

^o 14% of the self-condensation product, ethyl α -propionylpropionate, was obtained, b.p. 50-56° at 2.5 mm.; Y. Maroni-Barnaud and J. E. Dubois {Bull. Soc. Chim. France, 928 (1959)} reported b.p. 62-67° at 5.0 mm., ⁿ_D²⁰ 1.4225; H. D. Zook, W. J. McAleer, and L. Horwin {J. Amer. Chem. Soc., 68, 2404 (1946)} reported ⁿ_D²⁰ 1.4230.

^p Isolated as the potassium salt, (see expt. section).

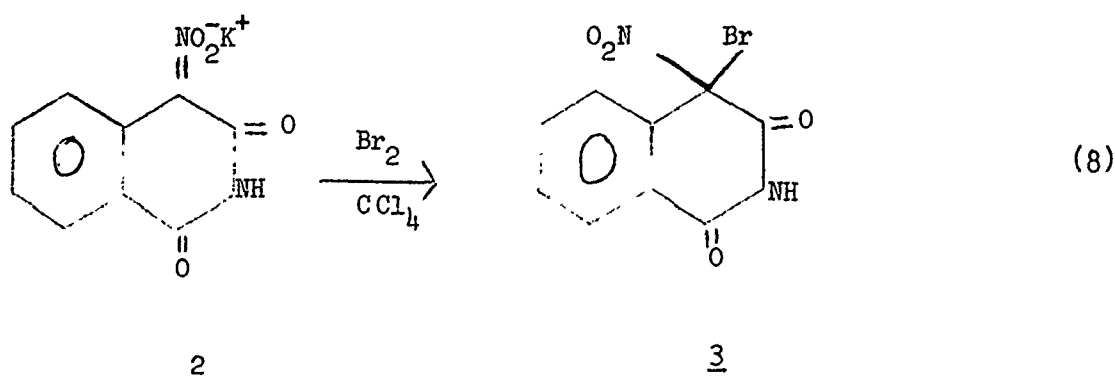
^q B.p. 97-99° at 0.17 mm., ⁿ_D²⁰ 1.5115; N. Kornblum, R. K. Blackwood, and J. W. Powers {J. Amer. Chem. Soc., 79, 2509 (1957)} reported b.p. 90-92° at 0.15 mm., ⁿ_D²⁰ 1.5098.

^r B.p. 54-57° at 0.2 mm.; lit. b.p. 90-92° at 3 mm., {Org. Syntheses, Col. Vol. II, p. 513}, ⁿ_D²⁰ 1.5323; M. Konowalow {Ber., 28, 1861 (1895)} reported ⁿ_D²⁰ 1.5323.

^s Isolated as potassium homophthalimidonitronate, (see expt. section).

^t o-Carbethoxy- α -nitrotoluene.

^u Approximately 35.5% of the starting ester was recovered.

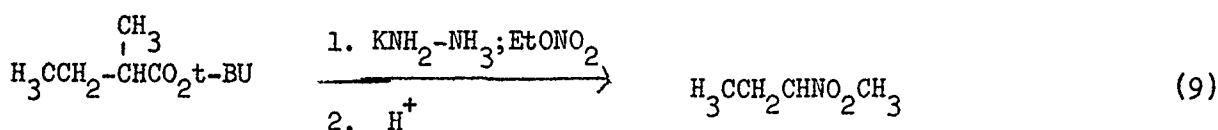


obtain a correct elemental analysis.

Aliphatic and Aryl Alkyl *t*-Butyl Esters

In general the *t*-butyl esters afforded higher yields of overall nitration than the ethyl esters, and no amide formation or self-condensation were observed (see Table VI).

The importance of salt formation can be seen in the nitration of *t*-butyl α -methylbutyrate which can only lead to an ester containing a tertiary nitro group. Cleavage was the predominant reaction and 2-nitrobutane was obtained in 72% yield (eq. 9). It has been previously observed that cleavage also predominated in the alkyl



nitration of cyclanones containing α -alkyl substituents*.

The *t*-butyl nitroesters were identified by correct elemental analyses and spectral data, which are detailed in Tables VII and VIII.

The infrared spectra of the α -nitroesters showed the characteristic carbonyl stretching vibration at $1745\text{-}1761\text{ cm}^{-1}$, and the nitro asymmetric stretching vibration at $1555\text{-}1575\text{ cm}^{-1}$ **. These absorption maxima constitute only a very small shift to

* H. Feuer and P. M. Pivawer, *J. Org. Chem.*, 31, 3152 (1966).

** The nitro symmetric stretching vibrations at $1370\text{ to }1390\text{ cm}^{-1}$ were masked by CH bending vibrations.

higher frequencies from their normal positions.* In the n.m.r. spectra of aliphatic α -nitroesters, the CHNO_2 absorption occurred at 4.8-5.2 ppm. In the n.m.r. spectra of aliphatic α -nitroesters, the CHNO_2 absorption occurred at 4.8 to 5.2 ppm. In the more acidic α -nitrophenylacetates this absorption was shifted down field to 6.1 to 6.2 ppm. (see Tables VIII and IX).

Study of the Cleavage and Transesterification Reactions

As already mentioned, the alkyl nitrate nitration of esters in the potassium amide-liquid ammonia system does not only lead to α -nitroesters and cleavage products, such as nitroparaffins, but also to transesterified α -nitroesters when the alkoxy groups of the ester and alkyl nitrate are different (eq. 7). Since very little information was available about the formation of these products, the course of these reactions was studied.

In a typical nitration, the alkyl nitrate is added to a mixture of ester and base at -33° and this is followed by acidification with gl. acetic acid at -50° after the ammonia had been replaced by ether.

The possibility that cleavage and (or) transesterification occurred during acidification was ruled out by the following experiments:

(1) treating the potassium salt of ethyl α -nitrocaproate (4) with an excess of gl. acetic acid in ethanol and ether gave only the nitro ester 4 in 91% yield. Careful analysis indicated that no cleavage products were present.

(2) when a mixture consisting of 72% compound 4 and 28% *t*-butyl α -nitrocaproate (5) was refluxed in an ethanolic acetic acid solution, the change in the ratio of 4 (70.5%) and 5 (29.5%) was negligible.

(3) distillation in vacuo at 0° prior to acidification of the reaction mixture from the nitration of ethyl caproate with ethyl nitrate gave one of the cleavage products, diethyl carbonate. After acidification of the residue, the other cleavage

* J. R. Dyer, "Applications of Absorption Spectroscopy of Organic Compound," Prentice-Hall, Inc., Englewood Cliffs, N. J., 1965, pp. 34-38.

Table VI

Alkyl Nitrate Nitration of t-Butyl Esters

Ester ^a $\text{RCH}_2\text{CO}_2\text{C}(\text{CH}_3)_3$	t-Butyl α -Nitroester, b,c Yield %	Ethyl α -Nitroester, c,d Yield %	Nitroparaffin, d,e Yield %	Total Nitration, f,g Yield %
$\text{n-C}_4\text{H}_9-$	21.7	33.1	32.5	87.3
C_2H_5-	22.1	30.8	24.5	77.3
CH_3-	25.5	22.0	14.0	61.5
H-	18.0	22.0 ^h	33.0 ^{i,j}	63.0
$\text{iso-C}_3\text{H}_7-$	33.2	17.5 ^{j,k}	26.0 ^{j,l}	76.7
$\text{CH}_3\text{CH}_2\text{CH}(\text{CH}_3)-$	0	0	72.0 ^{j,m}	72.0
C_6H_5-	35.6	3.2	49.0	87.8

^aNitrations were carried out in the presence of potassium amide-liquid ammonia at -33° with ethyl nitrate.

^bSee Table VII for physical properties.

^cEthyl and t-butyl α -nitroesters were obtained as a mixture and were separated by glpc.

^dExcept were noted physical constants are given in Table V.

^eThis is the expected cleavage product resulting from decarboxylation of the α -nitroester. In most cases the other product of decarboxylation, dialkyl carbonate, was not isolated.

Table VI (contd.)

f Total nitration represents the sum of t-butyl and ethyl α -nitroester, and nitroparaffin.

g Approximately 1-8% of the starting ester was recovered as a mixture of ethyl and t-butyl esters.

h n_D^{20} 1.4240; H. Feuer, H. B. Hass, and K. S. Warren {J. Amer. Chem. Soc., 71, 3078 (1949)} reported n_D^{20} 1.4252.

i B.p. 97-100°; lit. b.p. 101° {"Handbook of Chemistry and Physics," 39th ed., Cleveland Rubber Publishing Co., Cleveland, Ohio, 1957, p. 1039}.

j Glpc retention time was the same as that of an authentic sample.

k n_D^{20} 1.4272; N. Kornblum, R. K. Blackwood, and J. W. Powers {J. Amer. Chem. Soc., 79, 2509 (1957)} reported n_D^{20} 1.4269.

¹ B.p. 135-140°; E. Demole {Ann. Chem., 175, 144 (1875)} reported b.p. 137-140°.

m n_D^{20} 1.4060; R. Kuhn and H. Albrecht {Chem. Ber., 60, 1303 (1927)} reported n_D^{21} 1.4057.

Table VII

Physical Properties of *t*-Butyl α -Nitroesters

RCHCO ₂ C(CH ₃) ₃ NO ₂ R	Bp, °C (mm)	²⁰ n _D	Formula	Anal, %					
				Calcd			Found		
				C	H	N	C	H	N
<i>n</i> -C ₄ H ₉	65-68 (0.3)	1.4288	C ₁₀ H ₁₄ NO ₄	55.30	8.75	6.45	55.57	8.82	6.51
C ₂ H ₅	58-61 (1.6)	1.4229	C ₈ H ₁₂ NO ₄	50.78	7.99	7.40	50.99	7.98	7.60
CH ₃	45-47 (0.8)	1.4202	C ₇ H ₁₁ NO ₄	48.00	7.43	8.00	48.11	7.68	8.03
H	53-56 (1.4)	1.4245	C ₆ H ₁₁ NO ₄	44.72	6.83	8.69	44.86	6.84	8.57
<i>iso</i> -C ₃ H ₇	55-58 (0.5)	1.4262	C ₉ H ₁₃ NO ₄	53.20	8.37	6.89	53.47	8.57	6.99
C ₆ H ₅	101-102 (0.25)	1.4955	C ₁₂ H ₁₇ NO ₄	60.76	6.33	5.91	60.76	6.62	5.96

126

Table VIII

Spectral Data of t-Butyl α -Nitroesters

$\begin{array}{c} \text{RCHCO}_2\text{C}(\text{CH}_3)_3 \\ \\ \text{NO}_2 \end{array}$	Infrared Spectra, cm^{-1}		N.m.r. Spectra, ppm. ^a	
	<u>R</u>	<u>C=O</u>	<u>NO₂</u>	<u>CHNO₂</u> ^b
<u>n</u> -C ₄ H ₉		1754	1575	5.10 (t)
C ₂ H ₅		1751	1565	4.93 (t)
CH ₃		1745	1563	5.11 (q)
H		1754	1572	5.07 (s)
<u>iso</u> -C ₃ H ₇ ^c		1748	1563	4.79 (d)
C ₆ H ₅		1745	1575	6.12 (s)

^aDeuteriochloroform was the solvent with TMS serving as an internal standard.

^bMultiplicity; s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet.

^cThe ultraviolet spectrum was transparent above 230 m μ .

Table IX

Spectral Data of Ethyl α -Nitroesters

$\begin{array}{c} \text{RCHCO}_2\text{C}_2\text{H}_5 \\ \\ \text{NO}_2 \\ \text{R} \end{array}$	Infrared Spectra, cm^{-1}		N.m.r. Spectra, ppm. ^a
	C=O	NO_2	CHNO_2^b
$n\text{-C}_4\text{H}_9^c$	1754	1575	5.00 (t)
C_2H_5	1754	1575	5.05 (t)
CH_3	1754	1555	5.20 (q)
H	1761	1575	5.15 (s)
$\text{iso-C}_3\text{H}_7$	1754	1572	4.90 (d)
C_6H_5	1754	1565	6.21 (s)
$p\text{-CH}_3\text{OC}_6\text{H}_4$	1692 ^d	1524 ^d	^d

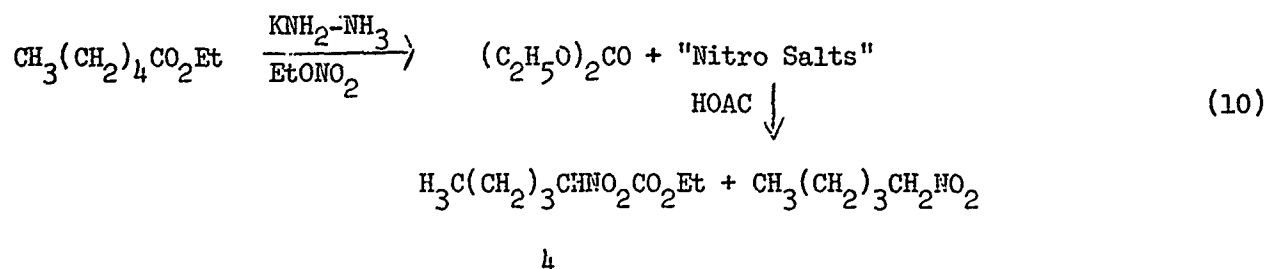
^aDeuteriochloroform was the solvent with TMS serving as an internal standard.

^bMultiplicity; s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet.

^cThe ultraviolet spectra was transparent above 230 m μ .

^dIsolated as the potassium salt.

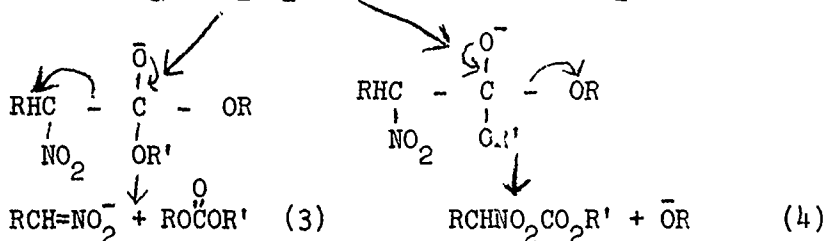
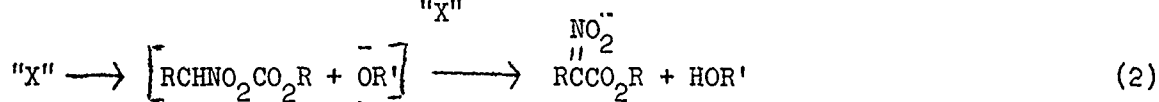
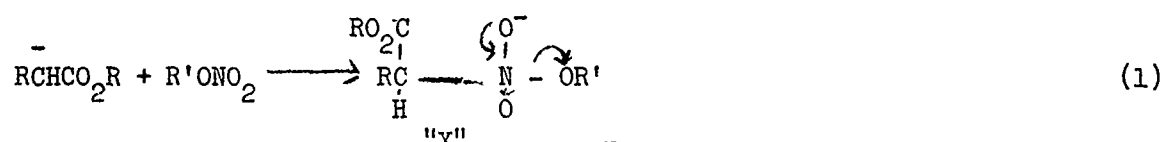
products, 1-nitropentane, and compound 4 were obtained, (eq. 10),



(4) alkyl nitration of ethyl p-methoxyphenylacetate without subsequent acidification gave in addition to a 72% yield of potassium α-carbethoxy-p-methoxyphenylmethanenitronate, a 21% yield of the cleavage product, potassium p-methoxyphenylmethanenitronate.

A possible reaction path for the alkyl nitration as presented in Scheme 1, involves the nucleophilic attack of a carbanion on the alkyl nitrate to give an intermediate "X" (step 1), which can collapse to a nitroester and an alkoxide ion (step 2). Direct alkoxide attack on the carbonyl group of the nitroester could then lead to cleavage (step 3), and (or) transesterification (step 4). This mode of attack has been previously reported to occur in the nitrosation* and nitration** of α-alkylated ketones.

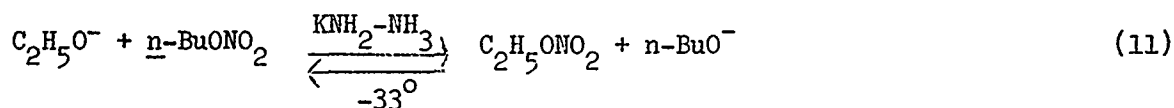
Scheme 1



* R. B. Woodward and W. E. Doering, J. Amer. Chem. Soc., **67**, 866 (1943).

** H. Feuer and P. M. Pivawer, J. Org. Chem., **31**, 3152 (1966).

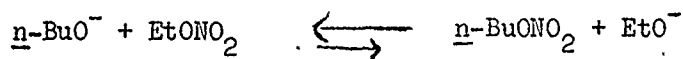
It appeared at first that support for this mechanism was obtained when it was established that the addition of potassium ethoxide prior to n-butyl nitrate during the nitration of t-butyl caproate resulted in the formation of n-butyl nitrocaproate (26.8%), ethyl α -nitrocaproate (4) (21.8%), and t-butyl α -nitrocaproate (5) (2.4%). However, it was ascertained in a control test that transesterification occurred at the conditions of the nitration reaction in the potassium amide-ammonia system between ethoxide ion and n-butyl nitrate to give n-butoxide ion and ethyl nitrate* (eq. 11). Thus a mixture of nitrating agents, ethyl, and n-butyl nitrate were present in the reaction mixture, and this could account for the formation of the ethyl and n-butyl α -nitroesters.**



* No transesterification occurred in the potassium t-butoxide-THF system between ethoxide ion and amyl nitrate at temperatures as high as 0°.

{H. Feuer and P. M. Pivawer, J. Org. Chem., 31, 3152 (1966)}.

** Surprisingly, only a trace amount of n-butyl α -nitrocaproate was obtained when potassium n-butoxide was added prior to ethyl nitrate during the nitration of t-butyl caproate. This difference might well be due to the low solubility of potassium n-butoxide in contrast to potassium ethoxide in the potassium amide-ammonia system. In fact, a control experiment between potassium n-butoxide and ethyl nitrate in the potassium amide-ammonia system did not lead to transesterification. Thus, the equilibrium between n-butoxide and ethyl nitrate lies far to the left.



Since it was established that ethoxide ion could be formed by the interaction of potassium amide and ethyl nitrate, it was considered possible that some of the t-butyl caproate was transesterified to the ethyl ester by reaction with ethoxide ion prior to nitration. In a control test it was found that ethyl caproate was formed to the extent of 23% when the t-butyl ester was treated with ethoxide ion in the potassium amide-ammonia system at the conditions of the nitration reaction.

So it is quite likely that some of the ethyl α -nitroester originated from the nitration of the ethyl ester.

But in any event, the formation of the ethyl α -nitroester was not due to direct alkoxide attack on the t-butyl α -nitroester (5), and this also seems to be the case with regard to the fragmentation reaction which gives rise to nitroalkane and dialkyl carbonate. The following experimental observations are pertinent:

(1) about 94% of ethyl α -nitrocaproate (4) was recovered on treatment at -33° in liquid ammonia with potassium ethoxide and subsequent acidification with gl. acetic acid at -50° .

(2) the potassium salt of 4 was prepared in 76% yield by adding 4 to an ethanolic potassium hydroxide solution at 0° . It should be pointed out that the nitration is carried out at -33° .

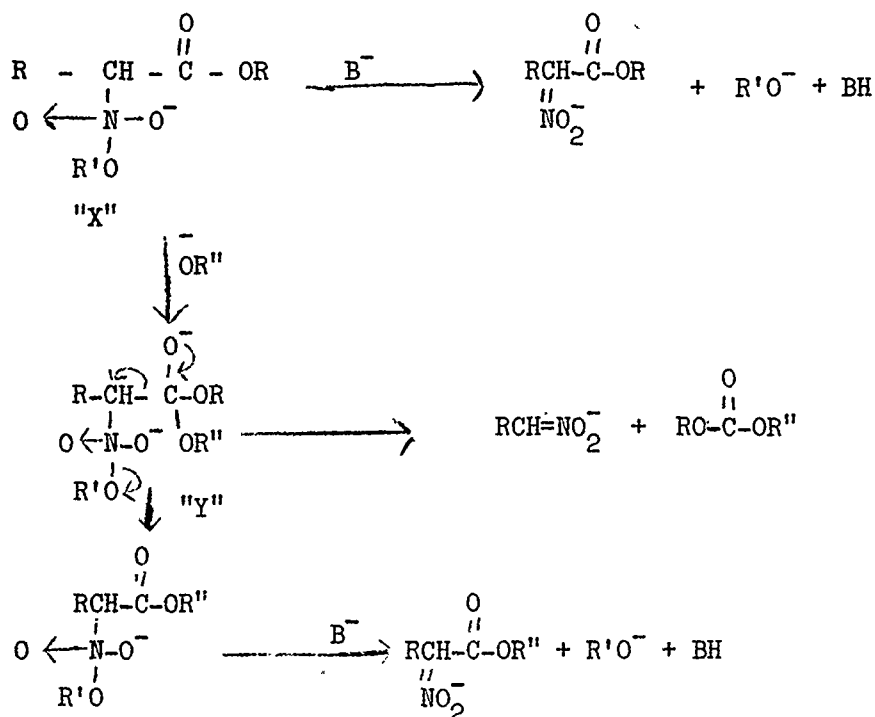
(3) when a mixture consisting of 4 (53%) and 5 (47%) was treated with potassium ethoxide in ammonia at -33° and then acidified with gl. acetic acid at -50° , the change in the ratio of 4 (51%) and 5 (49%) was negligible.

A mechanism which is consistent with our experimental observations and which can account for the fragmentation reaction involves nucleophilic attack by base* at the carbonyl group of intermediate "X", to give intermediate "Y", (Scheme 2). Fragmentation of intermediate "Y" leads then to cleavage. Intermediate "X" could also lead to the salt of the α -nitroester after abstraction of the α -hydrogen by base.

* Amide ion alkoxide ion or even the ester anion itself, can function as nucleophiles.

Intermediate "Y" if formed by alkoxide attack on "X", can also account for the formation of a transesterified α -nitroester, because if different alkoxides are involved, then collapse of intermediate "Y" can lead to a mixture of α -nitroesters.

Scheme 2



This mechanism can account for the fact that the ratio of α -nitroester was found to vary with the acidity of the starting ester. For instance, nitration of the more acidic ethyl phenylacetate gave a large ratio of cleavage product to α -nitroester than the less acidic *p*-methoxyphenyl acetate or ethyl caproate, (see Table V).^{*} At first sight it would be expected that the phenylacetates would give less cleavage product because the α -hydrogen being more acidic would be removed at

^{*} Considering per cent conversion, the ratio of cleavage product to α -nitroester in the alkyl nitration of ethyl phenylacetate, *p*-methoxyphenylacetate, and caproate was, respectively, 48% to 23%; 21% to 72%; and 18% to 58%.

a faster rate than nucleophilic attack would occur at the carbonyl group. But, apparently, the rate of proton removal and the nucleophilic attack at the carbonyl group are not competitive, and the better leaving group in intermediate "Y" will determine whether more nitroalkane or α -nitroester is formed.

EXPERIMENTAL

Alkyl Nitration of Ethyl Butyrate. - The following experiment is typical of the procedure employed. In an oven dried, nitrogen flushed, 500 ml. round-bottom, four-necked flask fitted with a Dry Ice condenser, thermometer, mechanical stirrer, and dropping funnel* were placed freshly cut potassium (4.10 g., 0.105 g. at.) and a catalytic amount of ferric nitrate in 300 ml. of anhydrous ammonia at -33° . After the potassium amide had formed, ethyl butyrate (11.05 g., 0.0995 mole) in 10 ml. of dry ether was added all at once. After stirring for 3-5 minutes, ethyl nitrate (14.30 g., 0.152 mole) in 5 ml. of dry ether was added as rapidly as possible (3-5 minutes** and the mixture stirred an additional 55 minutes at -33° . After the ammonia was replaced by ether, the reaction mixture was acidified at -50° with glacial acetic acid (20.0 g., 0.33 mole), and stirring was continued for 12 hours. The potassium acetate was filtered and the filtrate was evaporated. Distillation of the residue at 1.5 mm. gave ethyl α -nitrobutyrate (4), b.p. $58-61^{\circ}$, n_D^{20} 1.4238.

Extracting the residue which remained after distillation with pet. ether ($60-70^{\circ}$), and cooling the filtrate gave a white precipitate. Recrystallizing from a mixture of pet. ether ($60-70^{\circ}$) and chloroform (1:1) gave 0.6% (7%) butyramide, m.p. $115-116^{\circ}$. The material which had remained in the Dry Ice trap was redistilled at 70 mm. to give 1.95 g. (18%) starting ester, 1.24 g. (14%) 1-nitropropane and 0.12 g. (10%) diethyl carbonate as determined by glpc.

* The dropping funnel was provided with a side arm below the stopcock in order to allow the venting of ammonia.

** CAUTION! The first few drops of alkyl nitrate should be added slowly because a considerable exotherm develops.

Nitration of Ethyl Caproate without Subsequent Acidification. - Ethyl caproate

(14.0 g., 0.097 mole) was nitrated with ethyl nitrate (13.30 g., 0.146 mole) by the procedure described for 4 and the reaction mixture was distilled at 0° (1 mm.). Glpc analysis of the distillate showed the presence of diethyl carbonate (5.5%) and unreacted ester (5.3%).

Acidification of the residue at -50° with glacial acetic acid (20.0 g., 0.33 mole) and distillation gave two fractions. Fraction 1, b.p. 31-37° at 0.5 mm. contained 1-nitropentane (2.0 g., 17%) and unreacted ester (3.0 g., 21.4%), and fraction 2, b.p. 62-65° at 0.5 mm. was compound 4 (7.7 g., 41%) as determined by glpc.

Nitration of Ethyl p-Methoxyphenylacetate. - Ethyl p-methoxyphenylacetate (16.30 g., 0.084 mole) was nitrated with ethyl nitrate (11.45 g., 0.126 mole) by the procedure described for 4. Boiling off the ammonia and filtering the reaction mixture gave 21.6 g. crude nitro salts. Dissolving the solid material in hot isopropyl alcohol, filtering, cooling to room temperature, and crystallizing the precipitate from isopropyl alcohol gave 16 g. (72%) potassium α -carbethoxy-p-methoxyphenylmethanenitronate, m.p. 220-222° (dec.); $\lambda_{\text{max}}^{\text{Nujol}}$ 1692 cm^{-1} (C=O), 1524 cm^{-1} (C=NO₂), 1250 cm^{-1} (CH₃O), and 1175 cm^{-1} (C-O-C); n.m.r. (D₂O), 7.55-6.95 (C₆H₄, multiplet), 4.25 (CO₂CH₂CH₃, quartet), 3.86 (CH₃O, singlet), and 1.19 ppm. (CO₂CH₂CH₃, triplet).

Anal. Calcd. for C₁₁H₁₂NO₄K: C, 47.65; H, 4.34; N, 5.05; K, 14.08.

Found: C, 47.79; H, 4.27; N, 5.06; K, 13.91.

Placing the isopropyl alcohol filtrate in an ice chest and recrystallizing from the same solvent gave potassium p-methoxyphenylmethanenitronate (3.73 g., 21.7%), m.p. 198-201° (dec.); $\lambda_{\text{max}}^{\text{Nujol}}$ 1550 cm^{-1} (C-NO₂), 1250 cm^{-1} (CH₃O), and 835 cm^{-1} (C₆H₄); n.m.r. (D₂O), 8.05-6.85 (C₆H₄ and CHNO₂, multiplet) and 3.88 ppm. (CH₃O, singlet).

Anal. Calcd. for $C_8H_8NO_4K$: C, 46.83; H, 3.90; N, 6.83; K, 19.07; neut. equiv. 205.

Found: C, 46.38; H, 4.17; N, 6.39; K, 18.78; neut. equiv. 209.

Attempts to acidify the two nitro salts with either glacial acetic acid in ether or hydrogen chloride in ether led to decomposition as evidenced by evolution of oxides of nitrogen.

Nitration of Diethyl Homophthalate. - The experimental procedure was similar as described for the nitration of ethyl butyrate except that potassium (3.95 g., 0.101 mole), diethyl homophthalate (21.48 g., 0.091 mole), and ethyl nitrate (12.42 g., 0.136 mole) were employed. After acidifying at -50° with glacial acetic acid (20.0 g., 0.33 mole) and filtering, the precipitate consisted of potassium acetate and yellow solid "A".

After removing the ether from the filtrate, the residue was dissolved at 0° in an ethanol-potassium ethoxide solution (potassium 0.11 g., 0.028 mole in 50 ml. of absolute ethanol). Stirring the solution for 3 hours at 0° , removing the ethanol in vacuo, extracting the residue with ether, and removing the ether in vacuo gave unreacted ester (7.18 g., 35.4%).

Acidifying the residue (from the ether extraction) suspended in 50 ml. dry ether at 0° with glacial acetic acid (1.24 g., 0.021 mole) and stirring for 12 hours, gave after filtering off potassium acetate and removing ether in vacuo, o-carbethoxy- α -nitrotolnene (5.82 g., 30.6%), m.p. $50-51^\circ$, after crystallization from isopropyl alcohol; $\lambda_{\text{max}}^{\text{KBr}}$ 1724 (C=O) and 1570 cm^{-1} (NO_2); n.m.r. (CDCl_3), 8.2-7.2 (multiplet, C_6H_4); 5.80 (singlet, $-\text{CH}_2\text{NO}_2$), 4.30 (quartet, $-\text{CO}_2\text{CH}_2\text{CH}_3$), and 1.33 ppm. (triplet, $-\text{CO}_2\text{CH}_2\text{CH}_3$).

Anal. Calcd. for $C_{10}H_{11}NO_4$: C, 57.43; H, 5.26; N, 6.70.

Found: C, 57.43; H, 5.46; N, 6.64.

Solid "A" was washed copiously with water to remove the potassium acetate. Dissolving the residue in a minimum amount of warm 10% aq. potassium hydroxide,

adding methanol to the cloud point, and cooling in an ice chest gave after filtering and drying in vacuo potassium α -homophthalimidonitronate, m.p. 307° dec.; $\lambda_{\text{max}}^{\text{KBr}}$

3425 (NH), 1689 and 1661 (CONHCO), 1618 (C=NO₂), and 749, 700, 681 cm.⁻¹ (C₆H₄).

Anal. Calcd. for C₉H₅N₂O₄K: C, 44.25; H, 2.06; N, 11.46; K, 16.00; neut. equiv. 244.

Found: C, 44.21; H, 2.16; N, 11.57; K, 15.85; neut. equiv. 245.

Preparation of α -Bromo- α -nitrohomophthalimide. - Bromine was added at $3-5^{\circ}$ to potassium α -homophthalimidonitronate (0.33 g., 1.4 mmoles) in 20 ml. of dry carbon tetrachloride until the color of bromine just persisted. Evaporating the solvent in vacuo and recrystallizing the residue from carbon tetrachloride at 50° gave 0.32 g. (80%) α -bromo- α -nitrohomophthalimide, m.p. $110-112^{\circ}$; $\lambda_{\text{max}}^{\text{KBr}}$ 3390-3330 cm.⁻¹ (NH), 1709-1695 cm.⁻¹ (CONHCO), and 1580 cm.⁻¹ (NO₂); n.m.r. (CDCl₃), 9.3 (-NH), broad singlet and 8.4-7.6 ppm. (C₆H₄, multiplet).

Anal. Calcd. for C₉H₅N₂O₄Br: C, 37.93; H, 1.75; N, 9.82; Br, 28.03.

Found: C, 38.90; H, 1.85; N, 8.94; Br, 26.72.

Treatment of Ethyl α -Nitrocaproate (4) with Potassium Ethoxide at Alkyl Nitrate

Nitration Conditions. - To a potassium amide-ammonia solution, prepared from potassium (0.49 g., 12.6 mmoles), was added at -33° absolute ethanol (0.58 g., 12.6 mmoles). After stirring the mixture for 5 minutes, compound 4 (2.72 g., 14.4 mmoles) was added, stirring continued 1 hour and then the ammonia replaced by ether. Acidifying with glacial acetic acid (2.3 g., 38.0 mmoles) at -50° , stirring for 16 hours, removing potassium acetate, then ether, and subjecting the residue to glpc indicated that only IV was present (recovery 94% after distillation in vacuo).

Potassium 1-Carbethoxy-1-pentanenitronate. - To 1.24 g. (0.021 mole) of potassium hydroxide in 100 ml. of absolute ethanol at 0° was added ethyl α -nitrocaproate (4) (5.0 g., 0.0264 mole) and the mixture stirred 6 hours. Removing the ethanol in vacuo,

slurrying the remaining solid with dry ether, filtering, and drying in vacuo gave 4.15 g. (76%) potassium salt of 4, m.p. 137-141° (dec.); $\lambda_{\text{max}}^{\text{KBr}}$ 1689 cm^{-1} (C=O) and 1567 cm^{-1} (C=NO₂); n.m.r. (D₂O), 4.25 (O₂CCH₂CH₃, quartet) 2.6 (CH₂-CH₂C=NO₂⁻, triplet), and 1.4-0.9 ppm. (CH₃(CH₂)₂CH₂ and O₂CCH₂CH₃, multiplet).

Anal. Calcd. for C₈H₁₄NO₄K: C, 42.49; H, 6.17; N, 6.17; K, 17.18; neut. equiv. 227.

Found: C, 42.41; H, 6.31; N, 6.32; K, 16.95; neut. equiv. 230.

Conversion of Potassium Salt of 4 to Compound 4 at Alkyl Nitrate Nitration Conditions. -

To a mixture consisting of potassium salt of 4 (1.5 g., 6.6 mmoles) and absolute ethanol (0.3 g., 6.6 mmoles) in 50 ml. dry ether was added at -50° glacial acetic acid (0.9 g., 15.2 mmoles). After stirring the mixture for 16 hours, filtering, removing the solvent in vacuo, and distilling gave 1.14 g. (91.2%) of 4. Glpc analysis indicated that only compound 4 was present.

Alkyl Nitration of t-Butyl Caproate. - t-Butyl caproate (16.95 g., 0.0985 mole) dissolved in 5 ml. ether was added at -33° to 300 ml. ammonia containing potassium amide (10.85 g., 0.197 mole) (prepared in situ from potassium in the presence of Fe(NO₃)₃·10H₂O). After stirring the mixture for 3 minutes, ethyl nitrate (13.45 g., 0.148 mole) dissolved in 5 ml. of ether was added at -33° as fast as possible (3-5 minutes). Working up the reaction mixture as described in the preparation of ethyl α -nitrocaproate (4) gave two fractions, one containing 3.74 g. (32.4%) 1-nitropentane, b.p. 31-35° at 0.5 mm. The other fraction, b.p. 59-66° at 0.5 mm., consisted of 4.63 g. (21.7%) t-butyl α -nitrocaproate and 6.16 g. (33.1%) ethyl α -nitrocaproate as determined by glpc.

Addition of "Solid Potassium Ethoxide" Prior to Butyl Nitrate in Nitration of t-Butyl Caproate in Liquid Ammonia.*- To potassium amide (0.168 mole) in 300 ml. ammonia was added at -33° t-butyl caproate (14.45 g., 0.084 mole) in 10 ml. ether all at once. After stirring for 5 minutes, "solid potassium ethoxide" (10.58 g., 0.126 mole) was added at -33° . After stirring for 5 minutes, n-butyl nitrate (14.99 g., 0.126 mole) in 5 ml. of ether was added as rapidly as possible (3-5 minutes), and the reaction mixture stirred an additional 55 minutes at -33° . After the ammonia was replaced by ether and the mixture acidified at -50° with glacial acetic acid (40.0 g., 0.67 mole) stirring was continued for 14 hours. The potassium acetate was filtered and the ether removed in vacuo. Distillation of the residue gave three fractions which were analyzed by glpc. They contained 2.79 g. (28.4%) 1-nitropentane, b.p. $31-35^{\circ}$ at 0.5 mm.; 0.43 g. (2.4%) t-butyl α -nitrocaproate and 3.44 g. (21.8%) ethyl α -nitrocaproate (b.p. $61-67^{\circ}$ at 0.5 mm.); and 4.88 g. (26.8%) n-butyl α -nitrocaproate, b.p. $78-82^{\circ}$ at 0.5 mm., n_D^{20} 1.4342; $\lambda_{\text{max}}^{\text{Neat}}$ 1754 cm^{-1} (C=O) and 1570 cm^{-1} (NO_2); n.m.r. (CDCl_3), 5.11 ($\text{CH}_2\text{-CHNO}_2$, triplet), 4.22 ($\text{CO}_2\text{CH}_2\text{CH}_2$, triplet), and 2.5-0.8 ppm. $\{\text{CH}_3(\text{CH}_2)_3\text{CHNO}_2$ and $\text{CO}_2\text{CH}_2(\text{CH}_2)_2\text{CH}_3$, multiplet}.

Anal Calcd. for: $\text{C}_{10}\text{H}_{19}\text{NO}_4$: C, 55.30; H, 8.76; N, 6.45.

Found: C, 55.38; H, 8.80; N, 6.37.

The Dry Ice trap contained 0.12 g. (3.3%) of ethyl caproate as determined by glpc.

* "Solid potassium ethoxide" was prepared by adding potassium to excess absolute ethanol, removing ethanol in vacuo, and copiously washing the residue with ether.

CAUTION! The residue must not be dried because it tends to decompose explosively on exposure to air. It should be used immediately after washed with ether.

Treatment of a Mixture of Ethyl α -Nitrocaproate (4) and t-Butyl α -Nitrocaproate (5)

with Potassium Ethoxide at Alkyl Nitrate Nitration Conditions. - To a mixture of potassium amide prepared from potassium (0.36 g., 9.3 mmoles) in 50 ml. ammonia at -33° was added absolute ethanol (0.43 g., 9.35 mmoles). After stirring for 5 minutes, 2.0 g. of a mixture containing 53% compound IV and 47% compound V was added. After stirring at -33° for 1 hour, the ammonia was replaced by ether and the mixture acidified at -50° with glacial acetic acid (1.5 g., 25.0 mmoles) and stirred for 14 hours. Filtering the potassium acetate, removing the ether, and subjecting the residual liquid to glpc analysis showed the presence of 51% compound IV and 49% compound V.

Treatment of a Mixture of Compounds 4 and 5 with Ethanolic Acetic Acid. - To 200 ml. of a mixture consisting of 72% compound 4 and 28% compound 5 was added 50 ml. of absolute ethanol and 2 drops of glacial acetic acid, and the mixture heated at 60° for 16 hours. Subjecting the mixture to glpc analysis showed only the presence of 70.5% 4 and 29.5% of 5.

Conversion of t-Butyl Caproate to Ethyl Caproate in Potassium Amide-Liquid Ammonia Solution. - To a mixture of potassium amide prepared from potassium (2.27 g., 0.058 mole) in 100 ml. of ammonia at -33° was added t-butyl caproate (5.0 g., 0.029 mole) and the mixture stirred for 5 minutes. Then "solid potassium ethoxide" (3.70 g., 0.044 mole) was added with stirring for 5 minutes. Adding 6.4 g. (0.12 mole) anhydrous ammonium chloride, replacing ammonia by ether, filtering potassium chloride, removing ether in vacuo, and subjecting the residual liquid to glpc analysis showed the presence of 77% t-butyl caproate and 23% ethyl caproate.*

* In a control test, a mixture of t-butyl caproate and ethanol did not interact at the temperature of glpc analysis.

Transesterification Between n-Butyl Nitrate and "Solid Potassium Ethoxide" at Conditions of the Alkyl Nitrate Nitration. - To n-butyl nitrate (6.55 g., 0.055 mole) in 100 ml. of ammonia was added all at once at -33° , "solid potassium ethoxide" (4.62 g., 0.055 mole). After 5 minutes, the mixture was neutralized with anhydrous ammonium chloride (5.88 g., 0.11 mole), and after stirring 5 minutes at -33° , the ammonia was replaced by ether. Filtering the potassium chloride, concentrating the filtrate in vacuo and subjecting the residual liquid to glpc analysis showed the presence of n-butyl nitrate (88.8%) and ethyl nitrate (11.2%).

Subjecting a mixture of n-butyl nitrate and ethanol to glpc analysis showed that no transesterification occurred at the temperature of glpc injector block.